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ORGANIZATION OF Diencephalic and Brainstem Afferent Projections to the Lateral Septum in the Rat

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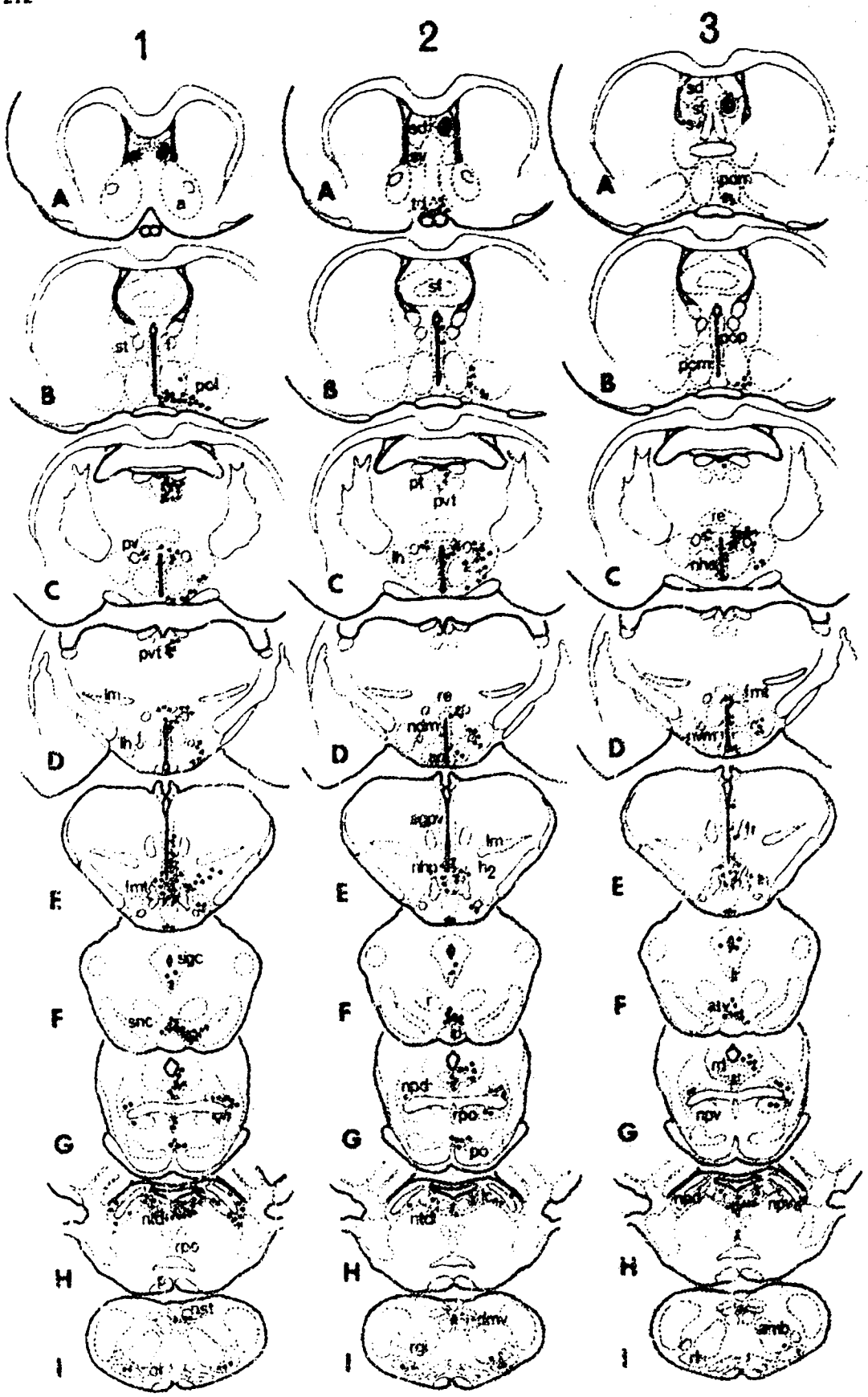
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Ascending diencephalic and brainstem afferents to the lateral septal column were studied by retrograde transport of horseradish peroxidase following microiontophoretic injections in the various subdivisions of the lateral septal area. Predominantly ipsilateral cells, of which several coincide with reported monoaminergic cell groups, appeared in the preoptic area, several hypothalamic nuclei, periventricular nuclei, raphe nuclei, pontine area and medulla oblongata. It is concluded that there is a heterogeneous monoaminergic input to the lateral septal area organized in a complicated pattern along the longitudinal axis of the lateral septum.

In a study on the neural substrate for control of food intake in the rat we found considerable numbers of somata labeled in the lateral aspects of the septal area subsequent to horseradish peroxidase (HRP) injections in lateral and ventromedial hypothalamic nuclei [9]. This led us to the conclusion that these hypothalamic centers, known to play a crucial role in control of feeding [12] and blood glucose homeostasis [17], receive a major input from the telencephalic limbic centers via the lateral septal area. This conclusion is supported by studies on effects of obesifying agents as bipiperidyl-mustard on central nervous structures. It was reported that these drugs, believed to eliminate parts of the neural control system of food intake, destroy cell populations in septum, ventromedial hypothalamus and motor vagus complex [6]. The importance of a septal-hypothalamic relation receives further support from studies dealing with the effects of septal stimulation on various modes of behavior, such as feeding, aggressive and sexual behavior [3, 14, 15]. In the present study we have attempted to gain a survey of the ascending brainstem sources that contribute input to the lateral septum and how these afferent projections are related to the various subdivisions of the lateral septum [18].

To solve this question in 21 male Wistar rats (approx. 300 g) we made small (200–300 μm) iontophoretic HRP deposits in various parts of the entire lateral



septum. The animals were adequately anesthetized with ether and placed in a Kopf stereotaxic apparatus. Glass micropipettes with tip diameters from 10 to 15 μm were filled with 10% HRP (Sigma VI) in 0.01 M NaCl and positioned according to König and Klippel coordinates [5]. The HRP was ejected iontophoretically (Midgard CS 3 current generator) with an interrupted (7 sec on – 7 sec off) positive current of 0.8 μA for 20 min total on-time. At 24 h after injection the animals were perfused with a buffered 0.5% paraformaldehyde, 1.5% glutaraldehyde solution. Brains were cut at 40 μm sections, processed for HRP according to the benzidine dihydrochloride method of De Olmos and Heimer [2] and counterstained with neutral red. It is worth mentioning that the superior quality of the precipitates can be saved from fading by storing the sections at low temperatures and protecting them from sunlight.

Differential retrograde labeling subsequent to injections in the various subdivisions of the lateral septum reflects a pattern of organization of ascending projections along the longitudinal axis of the septum. This differential pattern of afferent organization can be demonstrated by the result from three injections (Fig. 1), one at a rostral (Expt. 1), one at an intermediate (Expt. 2) and one at a caudal (Expt. 3) level in the lateral septum. These cases are representative for the results of 8 injections in the rostral zone, 7 injections at intermediate levels and 6 injections in the caudal zone of the lateral septum.

After lateral septal HRP injections labeled somata at the preoptic level were found in the more ventral aspects of the lateral and medial preoptic nuclei and a few cells in the preoptic periventricular nucleus. Medial preoptic labeling was most prominent after rostral septal injections, lateral preoptic cells appear to project to intermediate septal levels. More caudally, a vast number of cells in the dorsal thalamic periventricular and paratenial nuclei were labeled after rostral injections.

Fig. 1. Three series of transverse sections with the location of retrogradely labeled somata following HRP deposits in the rostral (series 1), intermediate (series 2) and caudal (series 3) zone of the lateral septal column. Each dot represents approx. 5 labeled somata. Abbreviations: amb, nucleus ambiguus; ar, arcuate nucleus; atv, ventral tegmental area of Tsai; dmV, dorsal vagal motor nucleus; f, fornix; fmi, fasciculus mamillothalamicus; fr, fasciculus retroflexus; h₂, field h₂ of Forel; ip, interpeduncular nucleus; lh, lateral hypothalamic area; lm, medial lemniscus; lr, nucleus linearis rostralis; ndm, dorsomedial hypothalamic nucleus; nha, anterior hypothalamic nucleus; nhp, posterior hypothalamic nucleus; npd, dorsal parabrachial nucleus; npv, ventral parabrachial nucleus; nst, solitary tract nucleus; ntd, dorsal tegmental nucleus; ntdl, dorsolateral tegmental nucleus; nvm, ventromedial hypothalamic nucleus; oi, oliva inferior; po, pons; pol, lateral preoptic nucleus; pom, medial preoptic nucleus; nop, periventricular preoptic nucleus; pt, paratenial nucleus; pr, magnocellular paraventricular nucleus; pvt, thalamic periventricular nucleus; r, nucleus ruber; rd, dorsal raphe nucleus; re, nucleus reuniens; rgi, gigantocellular reticular nucleus; rl, lateral reticular nucleus; rpo, rostral raphe nucleus; sd, dorsal part of lateral septum; sf, septum fimbrialis; sgc, central grey; sgpv, periventricular grey; sl, lateral septum; unc, pars compacta of substantia nigra; st, bed nucleus of stria terminalis; sv, ventral part of lateral septum; td, diagonal band of Broca.

This labeling was minimal after injections at more caudal septal levels. At the hypothalamic level differential labeling occurs bilaterally in the magnocellular part of the paraventricular nucleus. Although such cells were found labeled after all septal injections, labeling was most numerous after injection in caudal levels of the septum. Labeling in the lateral hypothalamus (lh) was most prominent after injections in the intermediate septal zone. After rostral injections labeling occurs in ventral lh and in bottom structures of the anterior hypothalamus known as the retrochiasmatic area. More caudally a limited number of reuniens cells reacted HRP-positive after rostral injections only, suggesting a reuniens projection confined to the anterior pole of the lateral septum. Always present after septal injections was a number of labeled perikarya around the fasciculus mammillo-thalamicus covering the dorsomedial hypothalamic nucleus reminiscent of cell group A13 [1, 4]. Few cells in the ventromedial nucleus became labeled after injections in the intermediate zone, as well as some arcuate cells after caudal injections. In the posterior hypothalamus a more or less continuous complex of labeled somata occurred in the periventricular grey, bilateral posterior hypothalamus, field h_2 of Forel, supramammillary commissure and lh. The number and extent of labeled cells in this complex was by far more conspicuous after injections of tracer in the rostral pole of the lateral septum.

Caudalwards labeling continues in the ventral tegmental area of Tsai (atv) and medial pars compacta of the substantia nigra. The nigral afferents only appear to project to anterior septal levels. Injections in the anterior level of the septum also resulted in the most numerous labeling in atv. More caudally afferent labeling occurred in dorsal, medial and pontal raphe nuclei with quantitative emphasis on labeling after more rostral injections. Labeled somata scattered bilaterally over ventral aspects of the periventricular nuclei appear in a rather unorganized pattern, but were especially prominent in the dorsolateral tegmental nucleus. Labeling of periventricular grey afferents, however, was minimal after caudal septal injections. Ipsilateral labeling in the dorsal tegmentum nucleus of Gudden as well as bilateral labeling in the locus coeruleus was observed after rostral injections only. At the pontine level, furthermore, tracer was found in somata of the dorsal and ventral parabrachial nuclei bilaterally. After rostral injections in the septum, the parabrachial labeling was most numerous. In those experiments labeling in the anterior pole of the npd extended laterally into the lateral lemniscus and more caudally even in the Kölliker-Fuse nucleus.

At the most caudal level of the medulla HRP-positive somata occurred in the dorsal motor vagus and solitary tract nuclei and ventrally in the lateral reticular nucleus without a clear correlation to the site of the injection.

The results described above allow two conclusive observations. Firstly, it is striking how various of the afferents labeled after septal injections coincide with the reported occurrence of monoaminergic (MA) cell groups [1, 4, 7, 12, 30]. Secondly, most of the afferents found appear to maintain a differential projection pattern

along the longitudinal axis of the lateral septal column. With regard to MA septal projections the present report for a great deal confirms a considerable amount of evidence from studies dealing with autoradiographic analysis of ascending MA projections [11, 16, 18, 19] or histochemical analysis of septal innervation [8, 10, 20]. Furthermore, it may be concluded that this MA septal innervation is organized in a rather complicated longitudinal pattern, suggesting differential monoaminergic modulation of septal input to the behavioral control elicited from the hypothalamus.

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